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EXAMINER	
BIANCHI, KRISTIN A	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
10/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,982	OKAYAMA ET AL.	
	Examiner	Art Unit	
	KRISTIN BIANCHI	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07/07/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *15-17 and 19-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 18* is/are rejected.

7)☒ Claim(s) *1-14 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/20/2005, 02/10/2006, 08/17/2006, and 03/28/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-22 are pending in the instant application. Claims 15, 16, 17, and 19-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected subject matter. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference which anticipates one group would not render obvious the other. Claims 1-14 and 18 are rejected. Claims 1-14 and 18 are objected.

Information Disclosure Statements

The information disclosure statements filed on October 20, 2005, February 10, 2006, August 17, 2006, and March 28, 2007 were considered and signed copies of form 1449 are submitted herewith.

Priority

Applicant cannot reply upon the foreign priority documents to overcome the rejections of this office action because a translation of said documents has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Election/Restrictions

Applicant's election with traverse of Group I and the compound of formula (I) wherein the compound of formula (1) is formula (c) in which Ar1 and Ar2 are pyridinyl in the response filed on July 7, 2008 has been acknowledged. The traversal is on the ground(s) that there is no burdensome search. This is not found to be persuasive because the inventions are independent and distinct because there is no patentable co-

action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

The requirement is still deemed proper and is maintained.

The scope of the elected subject matter and the search has been extended as follows:

The compounds of formula (I) (as depicted in claim 1) wherein Ar1 and Ar2 each independently represent a phenyl group which may have a substituent or a pyridyl group which may have a substituent and the rest of the variables are as described in claim 1.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter (i.e. compounds wherein Ar1 or Ar2 are any other 6-membered aromatic heterocyclic group) of claims 1-14 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to a non-elected invention. Therefore, the subject matter which are withdrawn from consideration as being non-elected subject matter differ materially in structure and composition and have been restricted properly because a reference which anticipates the elected subject matter would not render obvious the withdrawn subject matter and the fields of search are not co-extensive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formula (I) and salts thereof, does not reasonably provide enablement for solvates thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The state of the prior art/level of ordinary skill/level of predictability

Active pharmaceutical ingredients are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact, and generally stable format to store an active pharmaceutical ingredient or a drug product. Understanding and controlling the solid-state chemistry of active pharmaceutical ingredients, both as pure drug substances and

in formulated products, is therefore an important aspect of the drug development process. Active pharmaceutical ingredients can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals, and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability, and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms, such as polymorphs, solvates and hydrates, are not so common to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them, and evaluate their properties as valuable new pharmaceutical materials.

Therefore, for the reasons above, the state of the prior art is one of unpredictability.

As stated above, crystalline solids can exist in the form of polymorph, solvates or hydrates. "Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate, and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug. Hence, it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development" (Vippagunta et al., abstract).

In further discussing the predictability of the formation of solvates, Vippagunta et al. discloses that "predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds" (page 18, section 3.4).

The amount of direction or guidance present/existence of working examples

A disclosure should contain representative examples which provide reasonable assurance to one skilled in the art that the compounds which fall within the scope of a claim will posses the alleged activity. The specification does not adequately enable a method of making the solvates of the compounds that the claims encompass. Also, there is no data present or any working examples in the specification for the preparation of solvates of said compounds.

Breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any solvates of said compounds.

The quantity of experimentation needed

While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to prepare any solvate of said compounds.

The specification provides limited support, as noted above, for the solvates encompassed by the claims. The quantity of experimentation needed to make the

solvates encompassed by the claims would be an undue burden on one skilled in the chemical art, since the skilled artisan is given inadequate guidance for the reasons stated above. The science of crystallization has evolved such that, without guidance or working examples in the specification, the claim lacks enablement.

This discussion established *prima facie* non-enablement. Deletion of the word "solvate" from the claims would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 7, 9, 11, 14, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Asproni et al.

Asproni et al. discloses a compound **12n** (page 4657, Table 1) which is used in a pharmaceutical composition and anticipates a compound of the instant claims wherein formula (1) is formula (b), R2 is hydrogen, Ar1 and Ar2 are both phenyl, X is CO, A is a piperazine, and R1 is methyl.

Claims 1-3, 5, 7, 9, 11, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 03/027076.

WO 03/027076 discloses a compound (page 18, compound 87) which is used in a pharmaceutical composition and anticipates a compound of the instant claims wherein

formula (1) is formula (b), R2 is methyl, Ar1 and Ar2 are both phenyl substituted by chloride atoms, X is CO, A is piperidine, and R1 is hydroxyl.

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3, 5, 7, 9, 11, 12, and 18 are rejected under 35 U.S.C. 102(a) as being anticipated by US 2004/0063691.

US 2004/0063691 discloses a compound (page 12, Example 13) which is used in a pharmaceutical composition and anticipates a compound of the instant claims wherein formula (1) is formula (b), R2 is hydrogen, Ar1 and Ar2 are both phenyl substituted by chloride atoms, X is CO, A is piperidine, and R1 is an oxo group.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 5, 7, 10, 11, 12, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 2004/026301.

WO 2004/026301 discloses a compound (page 10, Example 35) which is used in a pharmaceutical composition and anticipates a compound of the instant claims wherein formula (1) is formula(c), Ar1 and Ar2 are phenyl groups which are substituted with chloride atoms, X is CO, A is piperidine, and R1 is piperidine.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 4, 6, 10-14, and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8 and 11-14 of copending Application No. 11/577,476. Although the conflicting claims are not identical, they are not patentably distinct from each other because the genus of the instant claims includes the Formula (I) of 11/577,476 wherein Ar1 and Ar2 independently represent a 6-membered aromatic heterocyclic group which may be substituted and R1 and R2 represent, together with the nitrogen atom substituted with R1 and R2, a 4- to 7-membered alicyclic heterocyclic group formed thereby. It would have been obvious to prepare the compounds of 11/577,476 (with Ar1 and Ar2 and R1 and R2 defined as above) given the instant application. Thus, the claims of 11/577,476 are *prima facie* obvious over the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 1-14 and 18 are objected for containing non-elected subject matter.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626

Kristin Bianchi
Examiner
Art Unit 1626

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